



ECDC Threat Assessment

West – Nile virus human infections in Romania, Italy and Hungary, 2008

30 October 2008

SOURCE AND DATE OF REQUEST

EWRS message posted by Romania, 9 September 2008

EWRS message posted by Italy, 23 September 2008

EWRS message posted by Hungary, 16 October 2008

PUBLIC HEALTH ISSUE

Neurological human cases of WN infection in Romania, Italy and Hungary: Plan of surveillance and blood donations

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DISEASE BACKGROUND INFORMATION

West Nile (WN) virus is a mosquito-transmitted virus whose reservoir is wild birds and mosquitoes. Humans are mainly infected through mosquito bites, although a few infection through organ transplantation and blood transfusion has been documented. Birds are amplifying hosts allowing the transmission of the virus to other biting mosquitoes, mostly from the *Culex* genus. Humans and horses are susceptible hosts.

After the infectious bite, an incubation period of 2–14 days precedes symptoms which tend to vary with the patient's age: from mild fever and malaise in children, a moderately severe disease in the young (high fever, red eyes, headache and muscle ache) to meningitis/brain infection in the elderly and the debilitated. No specific therapy is available.

The first large outbreak in humans in Europe happened in Romania in 1996. Previous evidence of WN transmission in Europe had been observed in the 1960-1970's in Southern and Central Europe (1). Since 1998, several outbreaks in horses have been

reported in Italy (Tuscany), France as well as sporadic humans in Romania, France, Portugal, Spain and Hungary (2,3). Other large epidemics were reported in Volgograd (Russia) in 1999, and in Israel in 2000. The WN virus suddenly emerged in North America in 1999 causing a high mortality in the native bird population and more than 10,000 fatalities in humans in the USA in the last nine years, mostly in the older age groups. It also spread rapidly to Central and South America but without a major impact in Public Health.

Due to the absence of clinical symptoms in more than 70% of the WN infection in humans, transmission via blood donations or organ transplants have occurred. No vaccine is currently available. The main preventive measures are aimed at reducing exposure to mosquito bite.

Events background

Romania

Two human cases of WN neuroinvasive illness have been reported:

- A 46 year old male, resident of Braila District (eastern part of Romania), with onset of disease on 3 August 2008, hospitalized on 8 August and confirmed on 3 September 2008,
- An 19 year-old resident of Bucharest, with onset of illness on 9 September 2008, hospitalized on 11 September and confirmed on 22 September. He had no history of travel outside the Bucharest area.

Both cases were confirmed by detection of specific WN IgM antibodies in cerebrospinal fluid (CSF), in the National Laboratory, Cantacuzino Institute.

In the last 10 years, 2 confirmed cases of WN infection have been registered in Braila district: in 1997 and 2001.

Italy

Three human cases of WN neuro-invasive illness have been reported in Bologna, Ferrara and Rovigo provinces (Emilia Romagna and Veneto regions) in an area where WN infection have occurred in horses and birds. The cases are:

- An 83 year old woman living in a small town in the province of Bologna, with onset of symptoms on 16 September and confirmed on 30 September by the Regional microbiological emergency reference center (CRREM) of Bologna and the Istituto Superiore di Sanita (ISS), Rome,
- A 59 year old man, living in Ferrara, confirmed on 20 October,
- An 81 year old woman living in Rovigo province (Veneto region), where WN infection have been reported in horses, with onset of symptoms on 29 August, hospitalized on 30 August 2008 with high fever and neurological symptoms. She was transferred to intensive care for severe conditions and she tested positive for WNV (IgM and IgG) on 27 October. Laboratory test confirmation is ongoing.

On 16 September 2008 WN virus infection in horses of several stables located in the province of Ferrara (Emilia Romagna region) were confirmed by the Istituto Zooprofilattico dell'Abruzzo e del Molise "G. Caporale". Meanwhile WN infection was detected in wild birds (magpies, crows...) from the same province, examined under the regional plan for wildlife monitoring (4). The area was considered at risk of infection with the on-going epizootic in horses and birds. On 30 October 2008, 68 out of 73 horses reported with clinical symptoms of WN infection have been confirmed in 26 farms in

Ferrara, Bologna Mantova, Rovigo, Padova and Venezia Provinces (5). Retrospective investigations indicated that first clinical symptoms in horses occurred on end August. WN virus had been previously reported in several horses in Tuscany region in 1998 (2).

Hungary

On 17 October 2008, 12 human cases (8 males and 4 females, mean age 52 ranging from 16 to 80 years) of WN infection including 11 neurological cases have been reported in Hungary from mid August to the end of September 2008 (week 33 to 39). Cases were confirmed by the Virális Zoonózisok Nemzeti Referencia-laboratóriumában (first report on September 19). The onset of the last diagnosed case was on 24 September. All patients recovered. These confirmed cases had no history of travel outside the country and recent blood donation (6). On 30 October 2008, 2 additional confirmed cases were reported, that is a total of 14 confirmed cases. Five additional cases are under laboratory confirmation and investigation.

Confirmed cases were widespread in 9 counties within the country. Additionally 10 to 15 horses with neurological symptoms compatible with a WN infection have been reported, but the diagnosis confirmation by PCR and immunochemistry is still pending (WN infection in animals is not a disease with notification). It seems that WN virus has been also identified in wild birds (hawk) in August-September.

West Nile had been reported in the past in Hungary with isolation from rodents and detection of antibodies in humans in the 1970's (2). Until 2003, WN virus infections in Hungary have never been associated with clinical symptoms (7). In late summer 2003, an outbreak of encephalitis emerged in a Hungarian goose flock and chronologically and geographically a serologically confirmed WN outbreak was also observed in humans, which involved 14 cases of mild encephalitis and meningitis (8).

With the decrease of the mosquito activity in the following weeks the risk of human exposure to mosquito bites is very low.

Active surveillance

In Italy, the risk analysis of the current situation is monitored and the multisectorial plan of active surveillance of WN disease was implemented in Emilia-Romagna (9). Suspect human cases of neuro-invasive illness in the region have to be reported, in addition to an active veterinary surveillance in horses and birds and specific vector control activities in the infected areas.

In Hungary and Romania, WN active surveillance has been implemented in addition with coordinated actions with their Ministries of Agriculture. Specific vector control activities were conducted in Bucharest on the end of September.

Blood donation

According to the EU Blood Directive 2004/33/EC (Annex III.2.2.1), donors shall be deferred from donation for 28 days starting from the day they left an area with ongoing transmission of WN virus to humans.

On 3 October 2008, the Italian National blood centre has requested all blood centres nationwide to defer for 28 days donors who have been for at least one night in the affected areas. Nucleic Acid Testing (NAT) has been introduced for the screening of blood donation on all donors resident in the provinces of Bologna and Ferrara.

In Hungary, the National Blood Service (Országos Vérellátó Szolgálat) has been informed about the cases. Blood donation restrictions have been implemented according to the national regulations in the affected areas (donation deferred for 28 days). In Romania, similar measures were taken.

Public Health Implications for Europe

With the onset of cooler weather as winter is approaching in the Northern hemisphere, the WN virus transmission is expected to halt soon.

The multidisciplinary approach (joining human, animal and environmental sectors) adopted by the Italian authorities for analyzing the risks in Emilia Romagna are a good example, which could be extended to other regions and countries.

Restrictive measures regarding blood donations were taken quickly in the concerned countries after the confirmation of the first human case. Information on the contamination and preventive measures was shared with the Blood Competent Authorities of the EU. The impact of blood donation restrictions on the supply of blood products would have to be measured.

ECDC would encourage the laboratory testing of WN human cases to seek confirmation in national reference laboratory.

Improving entomological investigations of the main vectors for WN virus, focusing on *Culex* species, would contribute to a better understanding of WN virus transmission. Any possible targeted vector control activities need to assess the impact of spreading of insecticides on the environment. Further elaboration on environmental measures to be adopted would be desirable.

Public awareness about the disease, mode of transmission and appropriate individual protection from mosquito bites mostly during the peak of mosquito activity (late in the day) is advisable in areas of ongoing West Nile virus transmission (10).

Despite the fact that WN virus is present in Europe since decades, further spread of WN virus and favorable environmental conditions for vectors may lead to larger geographical areas becoming affected and/or longer seasons of WN virus activity.

Member States may consider assessing and possibly developing preparedness for WN virus epidemics that involve larger numbers of human cases than seen at present, including the development of strategies for monitoring the safety of blood products (11,12). Cost-effectiveness depends on WN virus endemic in the geographical area and the cost of the testing. Targeted donor screening, use of a donor questionnaire and seasonal screening of blood units have been proposed to benefit cost-effectiveness. A number of parameters, e.g. length of season, number of samples included in a sample pool and definition of individuals at high-risk would need to be defined.

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